



Cervical Cancer Prevention

Francisco García, MD, MPH
Distinguished Outreach Professor
Obstetrics & Gynecology
Mexican-American Studies
Public Health
Pharmacy

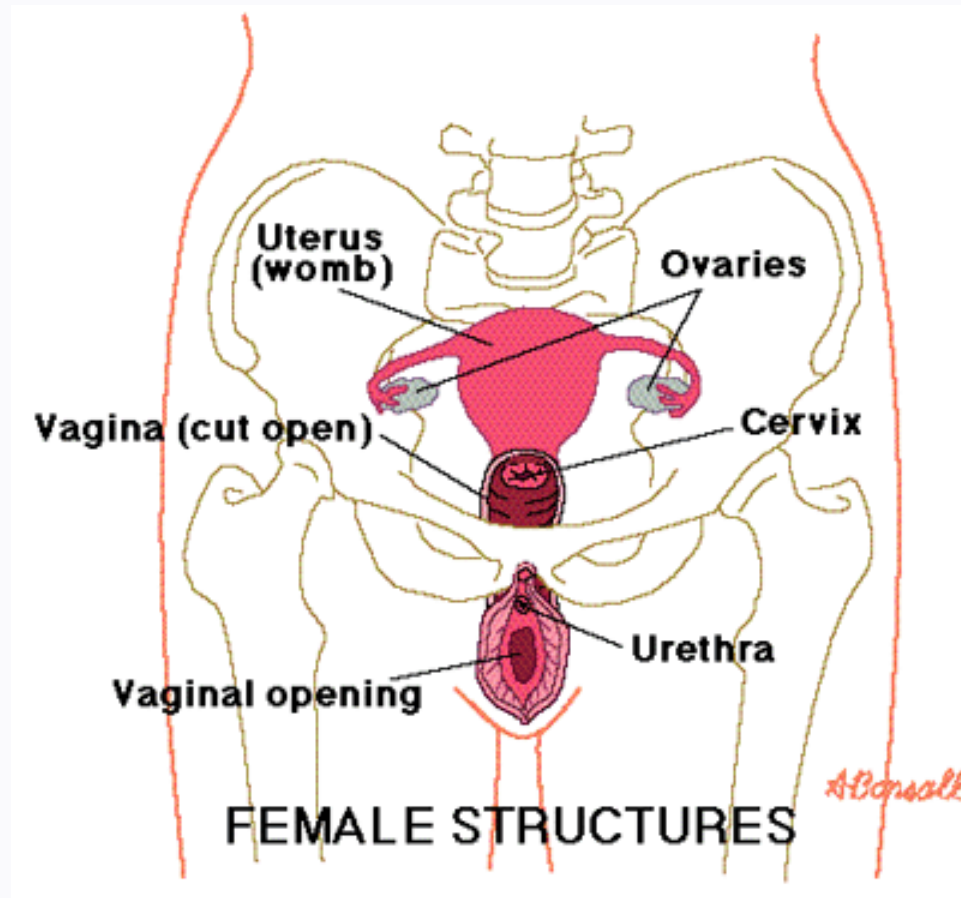
Objectives

- What is cervical cancer
- What causes cervical cancer
- How do you prevent cervical cancer

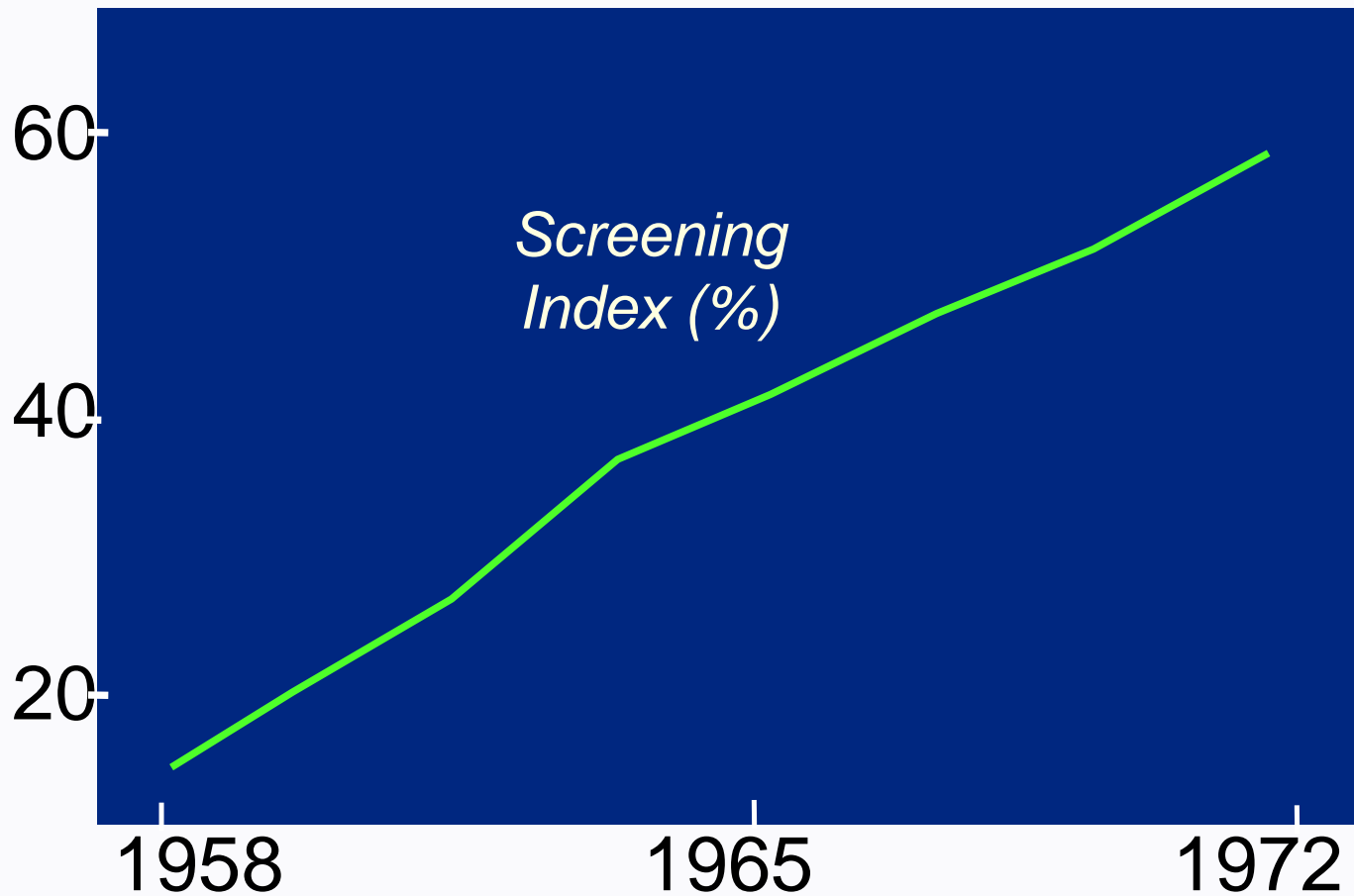
What is Cervical Cancer?

- Most common gynecologic malignancy worldwide
- US--about 10,520 new cases of invasive cervical cancer, and 3900 cancer deaths
- Disproportionately affects poor women and communities of color

The Cervix

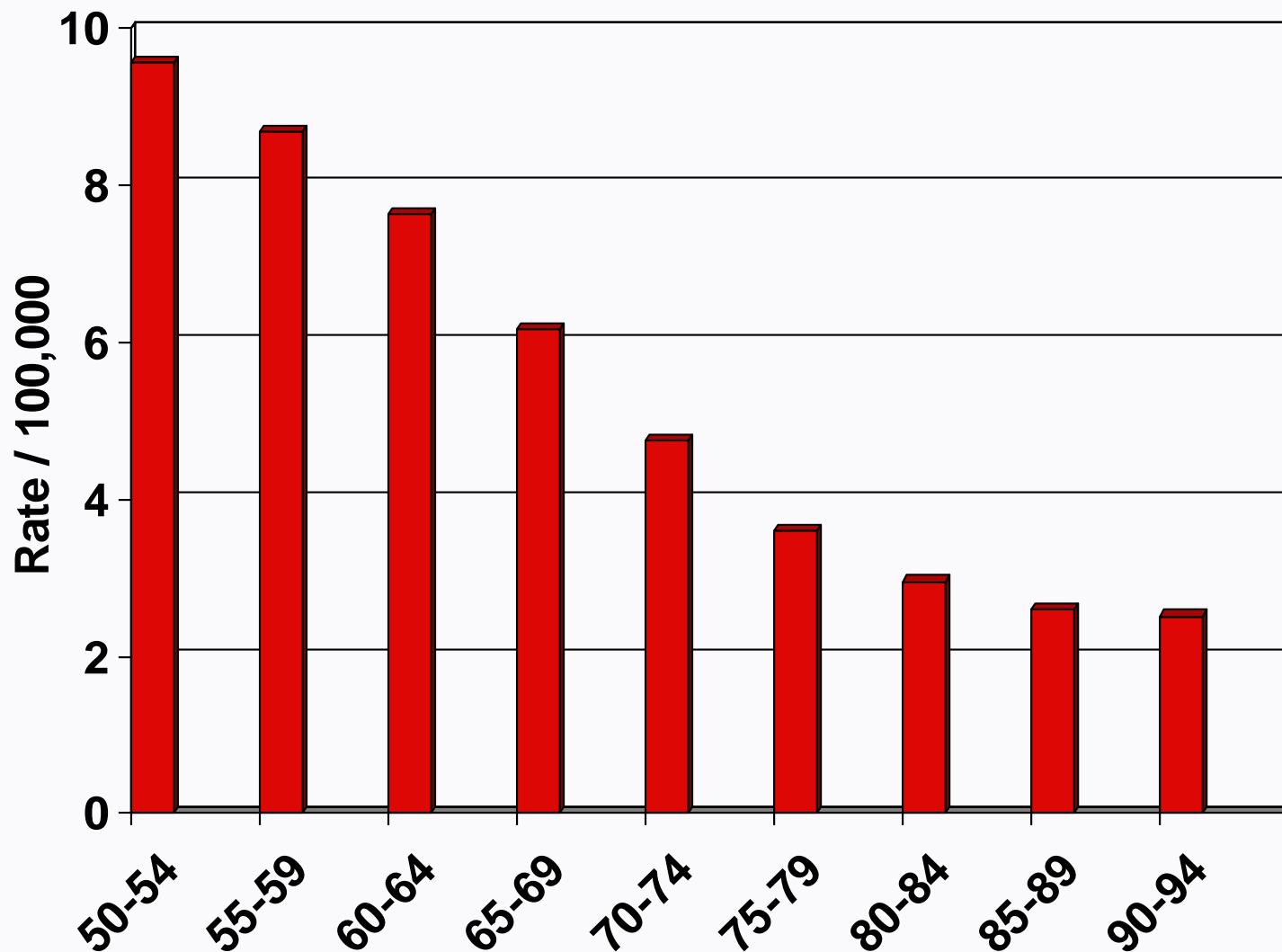


US Screening for Cervical Cancer



US cervix cancer mortality, 1950-94

5-year rates, white females



Cervical Cancer

- Life time risk 1/128
- 5 yr survival rate 73%
- Long pre-malignant disease
- Permits screening and early detection

Cervical Cancer

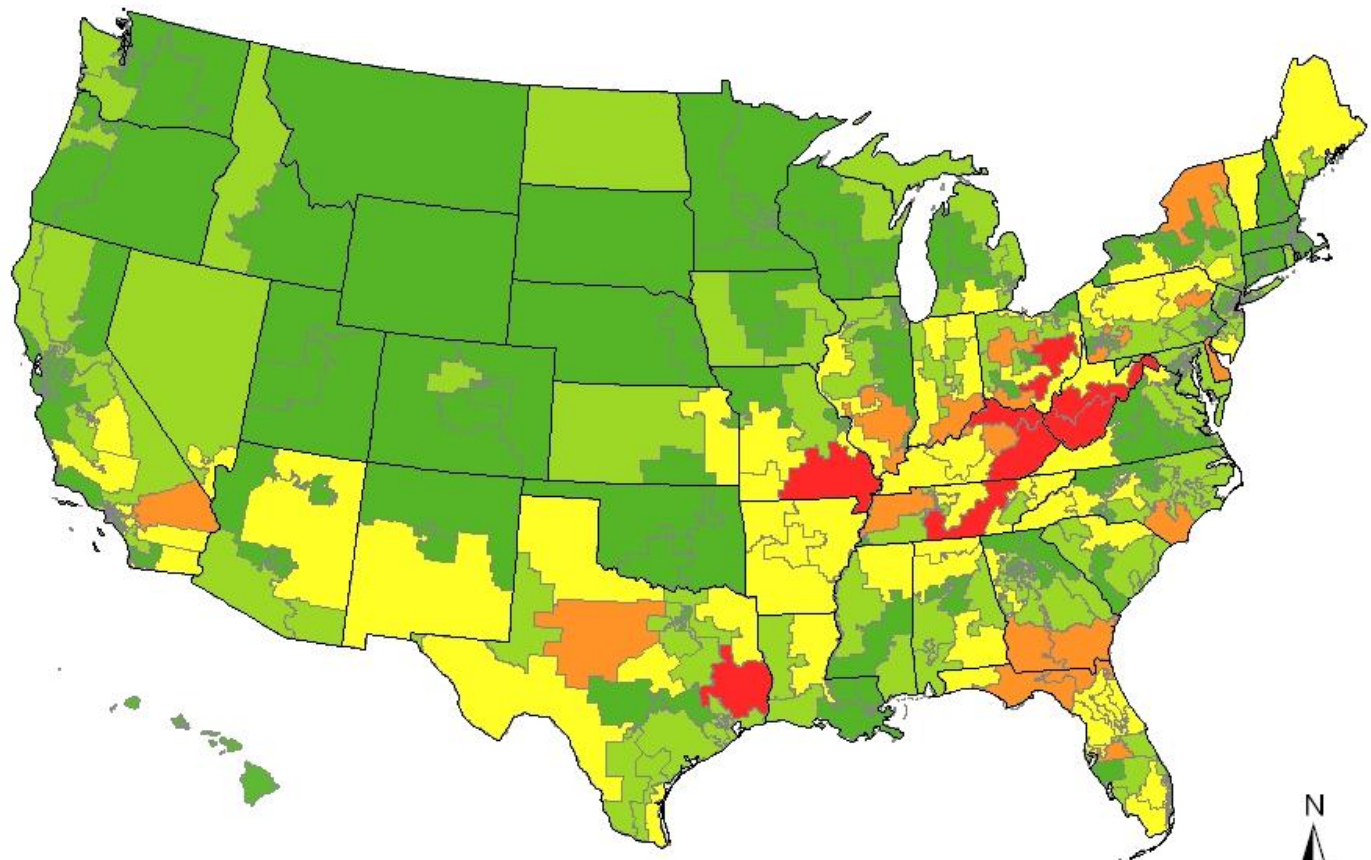
- Disproportionately affects poor women & women of color
 - 50% in woman who never had a pap
 - Occurs twice as likely among Hispanics (14.8/100k v. 8.4/100k among whites)
 - More likely have advanced stage/invasive disease
 - pre-malignant disease
 - More likely die from cervical cancer

Cervical cancer mortality rates 1990-2001

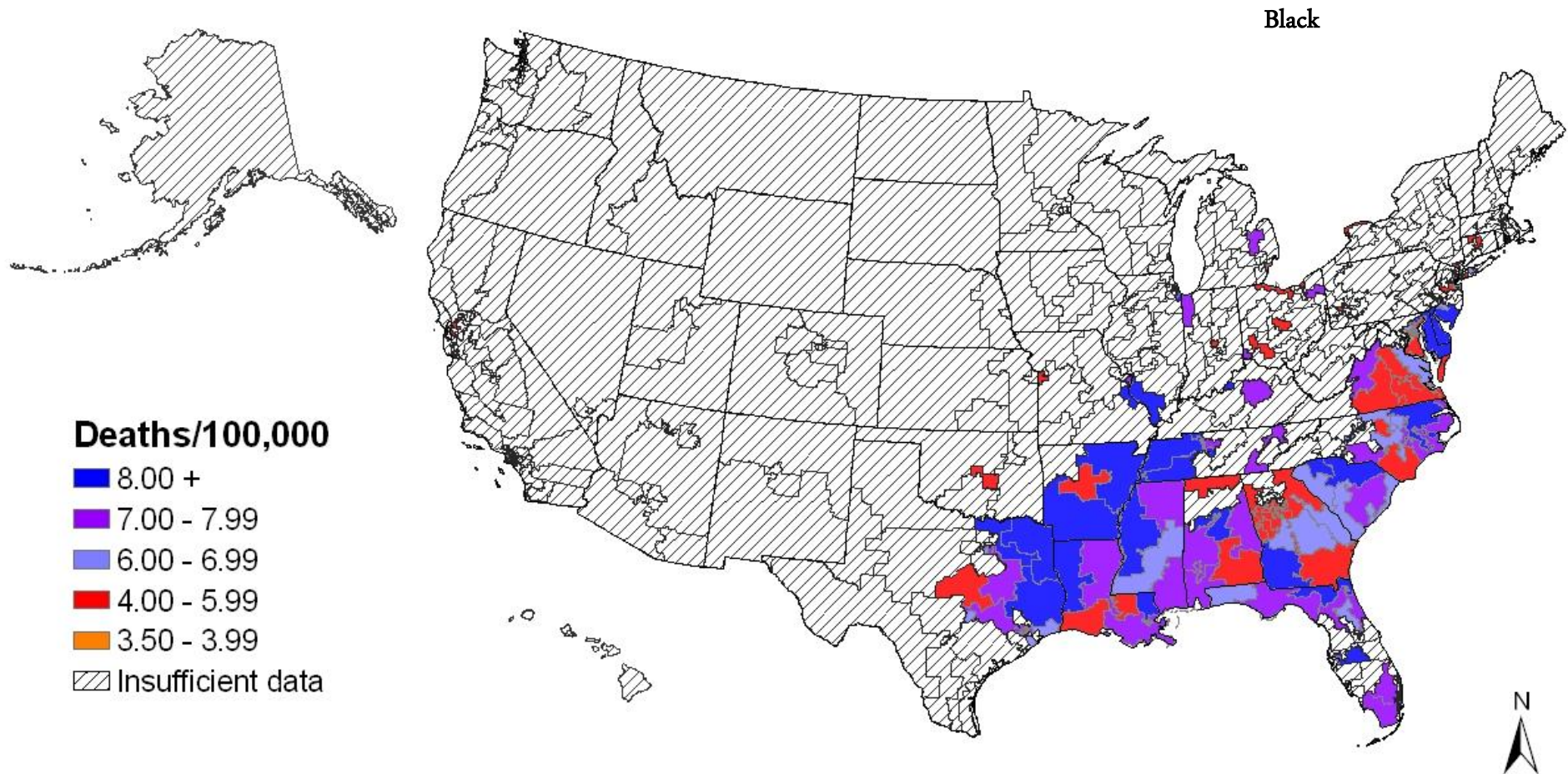
White Non-Hispanic Population

Deaths/100,000

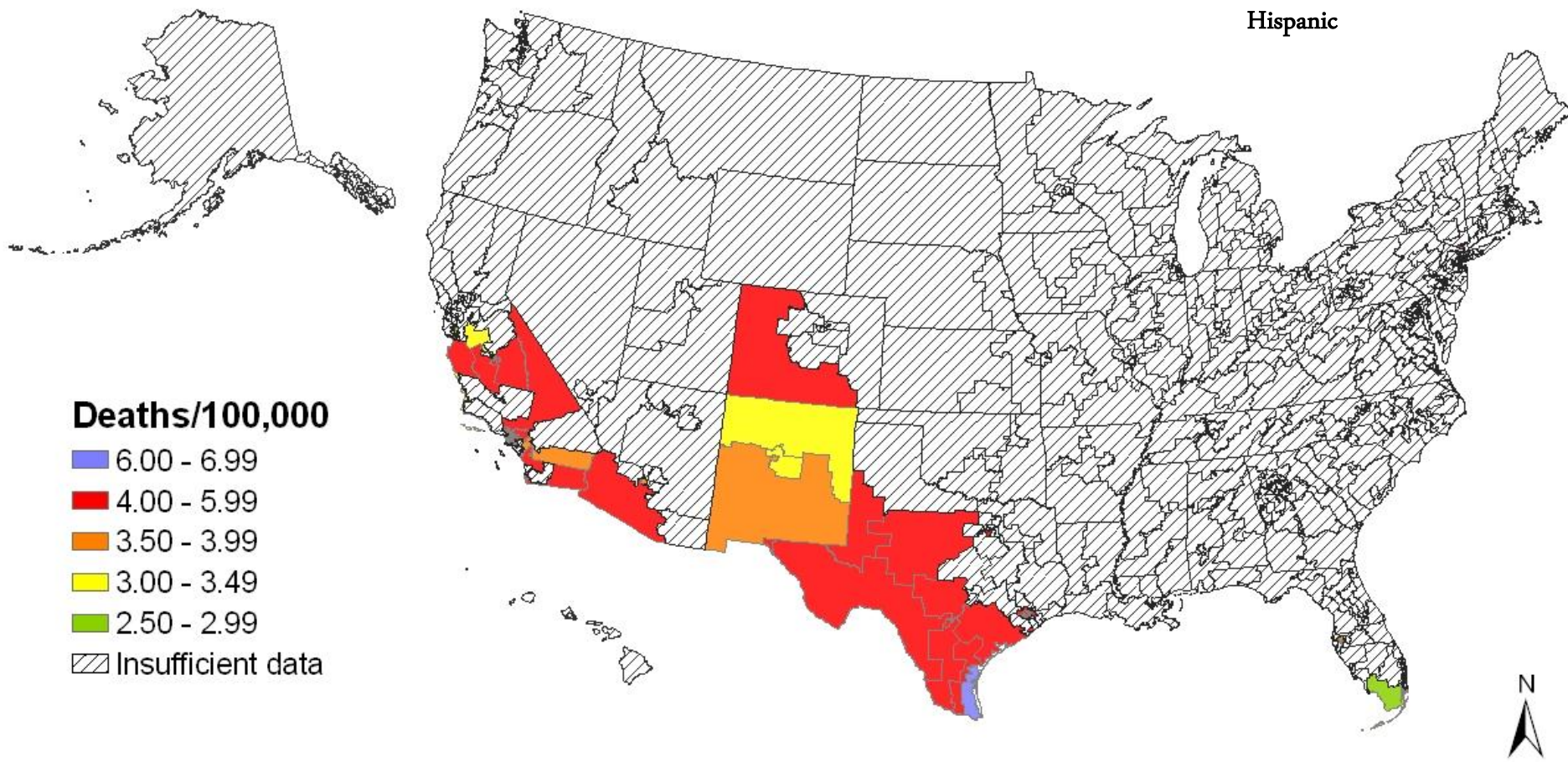
- 4.00 - 5.99
- 3.50 - 3.99
- 3.00 - 3.49
- 2.50 - 2.99
- < 2.50



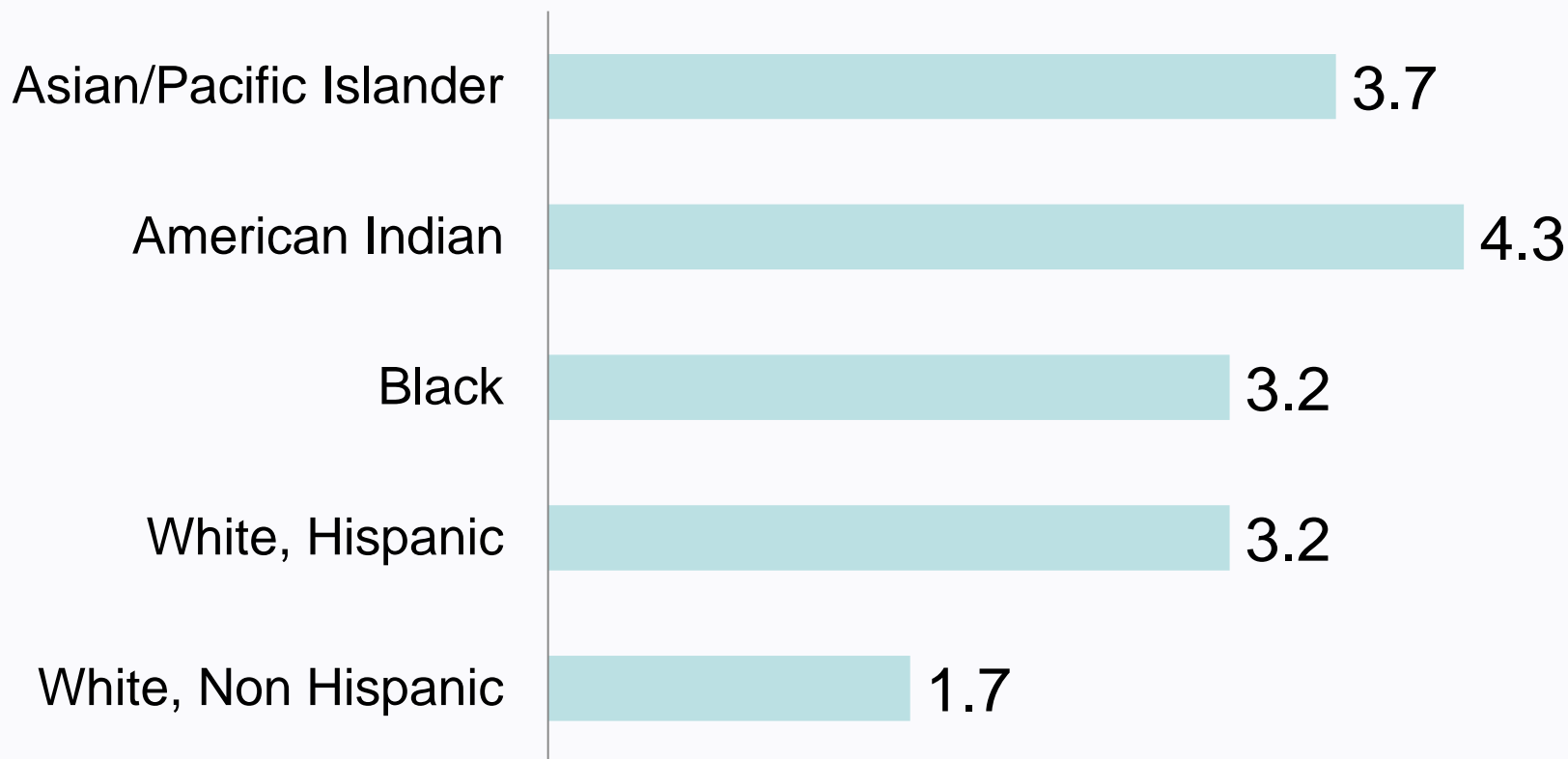
Cervical cancer mortality rates 1990-2001



Cervical cancer mortality rates 1990-2001

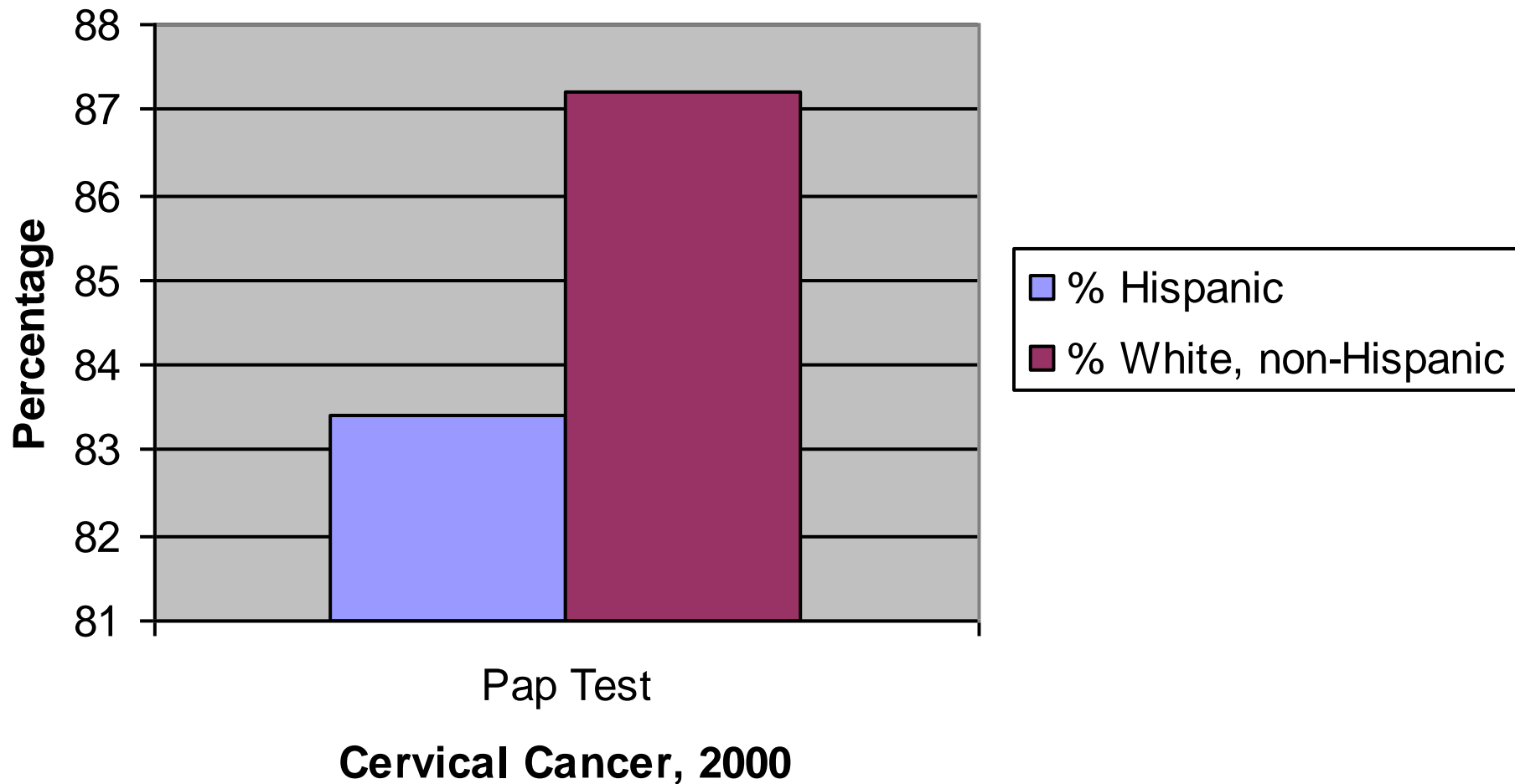


AZ Cervix Cancer Mortality 2001-2004

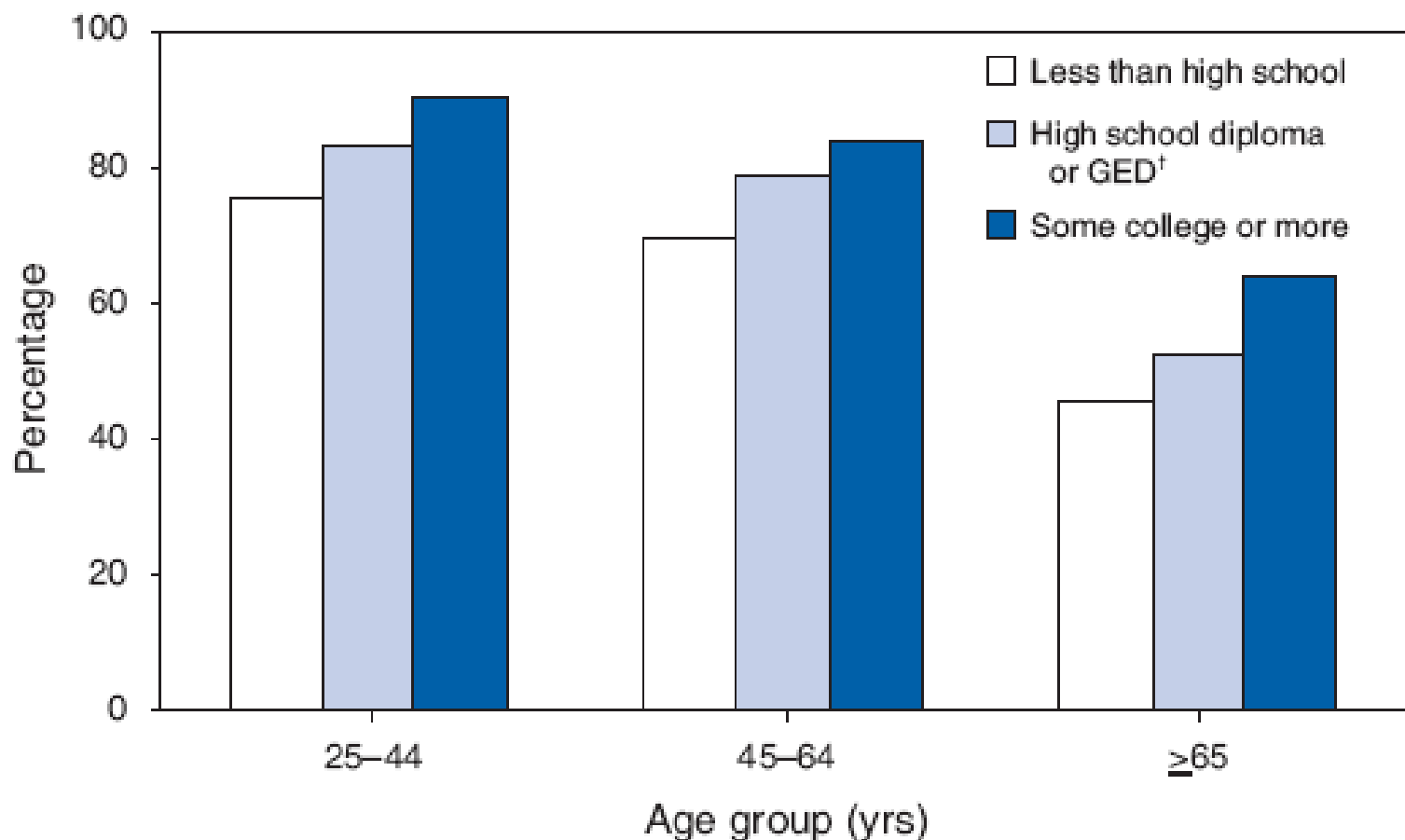


■ Age-Adjusted rate per 100,000 population

Cancer Screening Examinations, Adults, by American Cancer Society Guidelines, 2000 and 2001



Percentage of Women Aged Who Had a Pap During the Preceding 3 Years, by Age Group and Education Level --- NHIS, 2005



Cervical Cancer & Pap Smear Screening

- 50-60% are due to a failure to screen
- 10-15% due to inappropriate follow-up
- 35% are errors in sampling / evaluation

15 - 30% = sampling error

5 - 20% = screening error

What causes cervical cancer?

What is HPV?

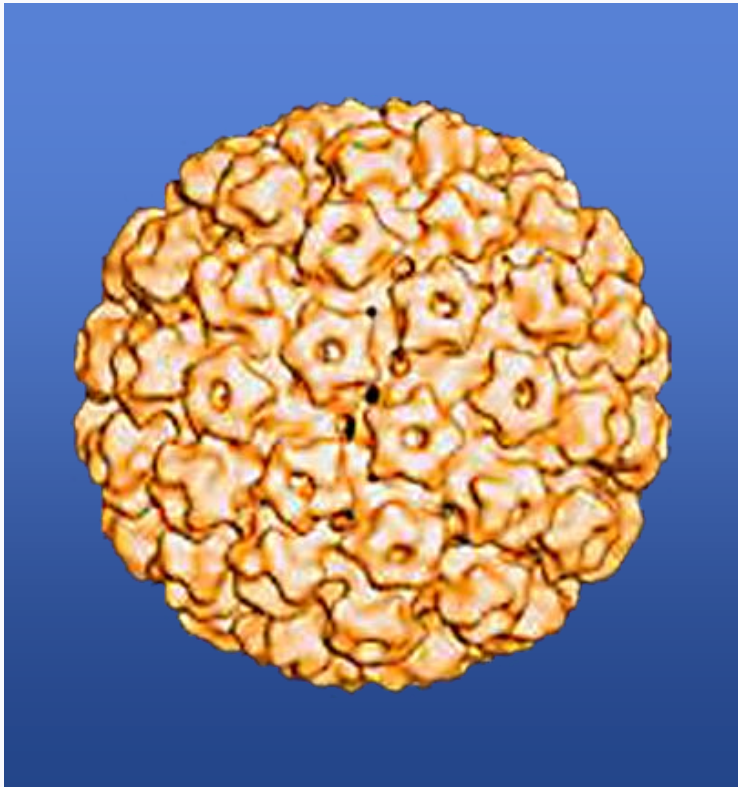
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HPV

Non-enveloped double-stranded DNA virus¹



- >100 types identified²
- 30–40 anogenital^{2,3}
 - 15–20 oncogenic^{*,2,3} types (16, 18, 31, 33, 35, 39, 45, 51, 52, 58⁴)
 - HPV 16 (54%)/HPV 18 (13%) account majority of cervical cancers⁵
 - Nononcogenic[†] types (6, 11, 40, 42, 43, 44, 54)⁴
 - HPV 6/11 are most often associated with external genital warts.³

*High risk; †Low risk

1. Howley PM. In: Fields BN, Knipe DM, Howley PM, eds. Philadelphia, Pa: Lippincott-Raven; 1996:2045–2076.
2. Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934.
3. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis*. 2002;35(suppl 2):S210–S224.
4. Muñoz N, Bosch FX, de Sanjosé S, et al. *N Engl J Med*. 2003;348:518–527.
5. Clifford GM, Smith JS, Aguado T, Franceschi S. *Br J Cancer*. 2003;89:101–105.

US HPV Statistics

- Lifetime risk for sexually active men/women is $\geq 50\%$ ¹
- By 50 yoa, >80% of women acquired genital HPV infection¹
- Estimated incidence: 6.2 m/ year¹
- Estimated prevalence: 20 m²
- In sexually active individuals 15–24 years of age, ~9.2 m currently infected.³
 - 74% new HPV infections in this age group.³
 - Among women <25, prevalence rates ranged from 28% to 46%.^{4,5}

1. Centers for Disease Control and Prevention. Rockville, Md: CDC National Prevention Information Network; 2004.

2. Cates W Jr, and the American Social Health Association Panel. *Sex Transm Dis*. 1999;26(suppl):S2–S7. 3. Weinstock H, Berman S, Cates W Jr. *Perspect Sex Reprod Health*. 2004;36:6–10. 4. Burk RD, Ho GYF, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis*. 1996;174:679–689. 5. Bauer HM, Ting Y, Greer CE, et al. *JAMA*. 1991;265:472–477.

Common HPV Types Associated With Benign & Malignant Disease

HPV Types

Manifestations

Low-Risk

6, 11, 40, 42,
43, 44, 54, 61,
70, 72, 81

Benign low-grade
cervical changes

Condylomata acuminata
(Genital warts)

High-Risk

16, 18, 31, 33,
35, 39, 45, 51,
52, 56, 58, 59,
68, 73, 82

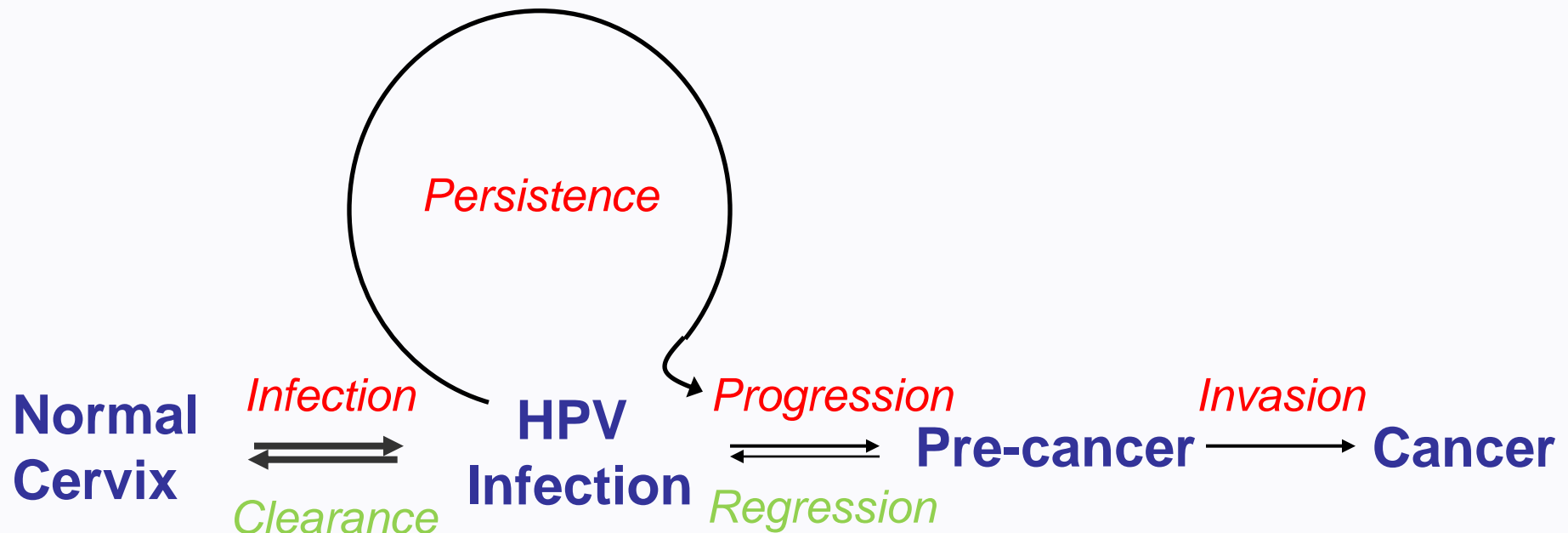
Low-grade cervical changes

High-grade cervical changes

Cervical cancer

Anogenital and other cancers

Natural History of HPV & Cervical Cancer



HPV and Cancer¹

Cancer	% Associated With Certain HPV Types
Cervical*	≥95%
Vaginal*	50%
Vulvar*	>50%
Penile	50%
Anal	>70%
Oropharyngeal	20%
Non-melanoma ski	90% [†]

*Includes cancer and intraepithelial neoplasia

[†]Immunocompromised patients

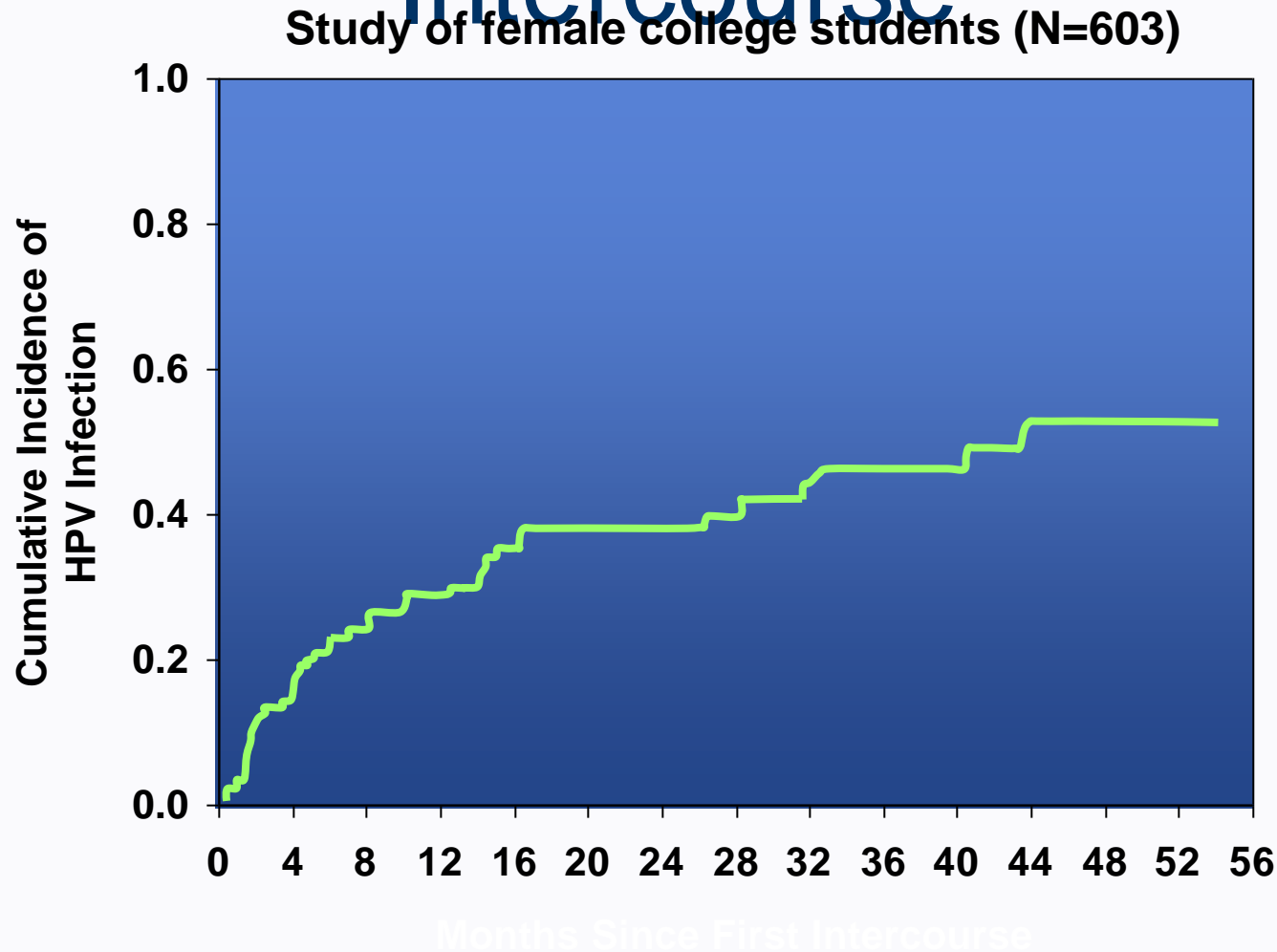
1. Gonzalez Intxaurraga MA, Stankovic R, Sorli R, Trevisan G. *Acta Dermatovenerol.* 2002;11:1–8.

How do you get HPV?

- Sexual contact
 - Sexual intercourse¹
 - Genital–genital, manual–genital, oral–genital^{2–4}
 - Genital HPV infection in “virgins” rare, may result from nonpenetrative sexual contact²
 - Condom use may reduce risk, but not fully protective²
- Nonsexual routes
 - Mother to newborn (vertical transmission; rare)⁵
 - Fomites, theoretical (undergarments, surgical gloves, medical instruments)^{6,7}

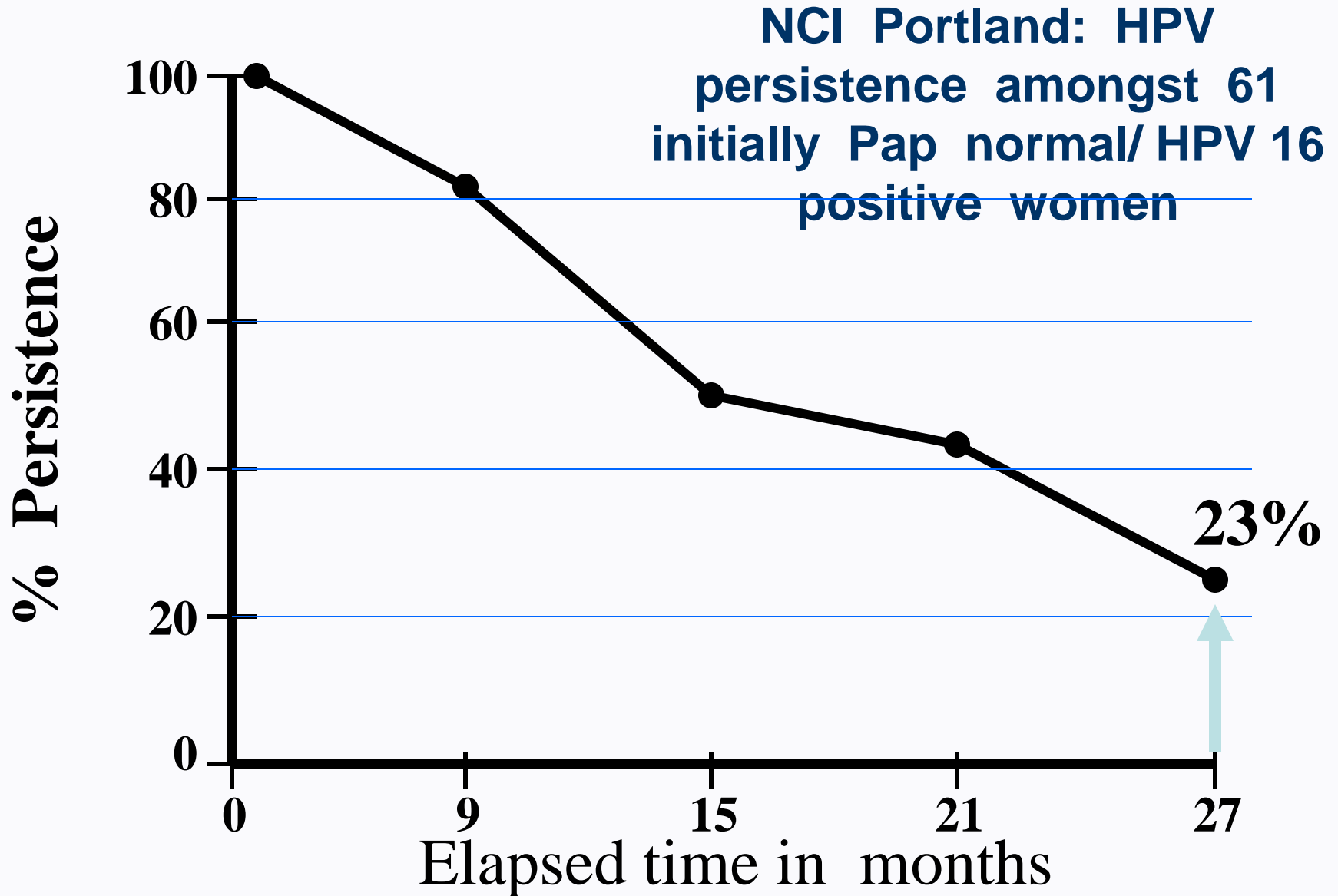
1. Kjaer SK, Chackerian B, van den Brule AJC, et al. *Cancer Epidemiol Biomarkers Prev.* 2001;10:101–106. 2. Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. *Am J Epidemiol.* 2003;157:218–226. 3. Fairley CK, Gay NJ, Forbes A, Abramson M, Garland SM. *Epidemiol Infect.* 1995;115:169–176. 4. Herrero R, Castellsague X, Pawlita M, et al. *J Natl Cancer Inst.* 2003;95:1772–1783. 5. Smith EM, Ritchie JM, Yankowitz J, et al. *Sex Transm Dis.* 2004;31:57–62. 6. Ferenczy A, Bergeron C, Richart RM. *Obstet Gynecol.* 1989;74:950–954. 7. Roden RBS, Lowy DR, Schiller JT. *J Infect Dis.* 1997;176:1076–1079.

Infection From Time of First Intercourse



From Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. Genital human papillomavirus infection: Incidence and risk factors in a cohort of female university students. *Am J Epidemiol.* 2003;157:218–226, by permission of Oxford University Press.

Most HPV infections are transient



How do you prevent cervical cancer?

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What is a Pap Smear?

- Sampling of the cells on the surface cervix
- Collected to “screen” for cervical cancer and its precursors
- Requires a pelvic examination and the capability to process the specimen
- Usually occurs annually

Thin-layer Preparations

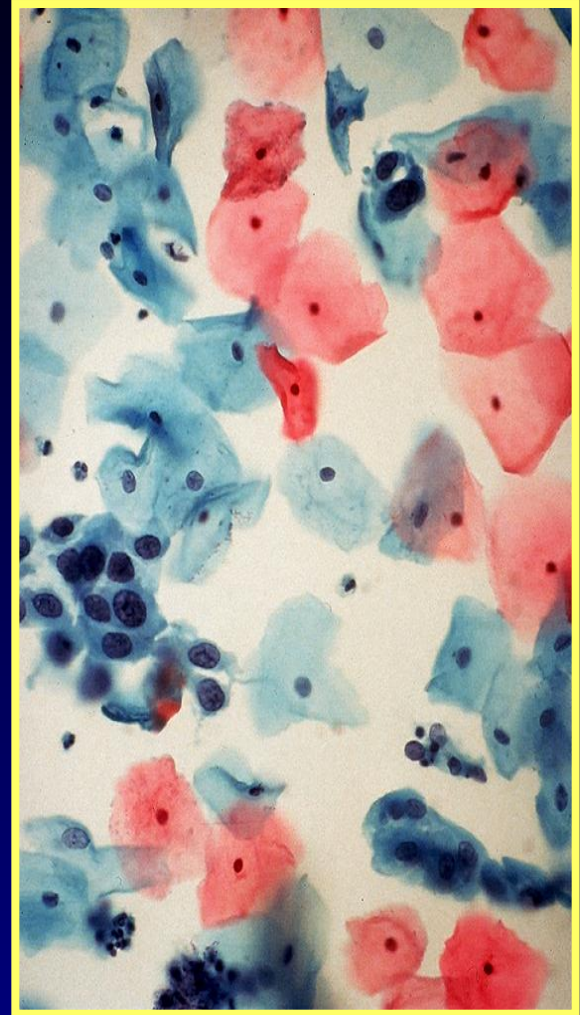
Conventional Pap



AutoCyte PREP



Thin-Layer Cytology Preparation



ACS Guidelines

- When to start screening
 - 3 years after onset vaginal intercourse
 - No later than 21 yoa

ACS Guidelines

- When to discontinue screening
 - ≥ 70 , with cervix, three normal and no anbl paps in 10yrs
 - Screen prev unscreened
 - Prior screening results unknown
 - H/O cancer, in utero DES, immunocompromised
 - HPV positive

ACS Guidelines

- Screening interval
 - Annual with conventional cytology OR
 - Every 2 years with liquid-based cytology
 - If ≥ 30 yoa, 3 consecutive normal paps, may screen every 2-3 years

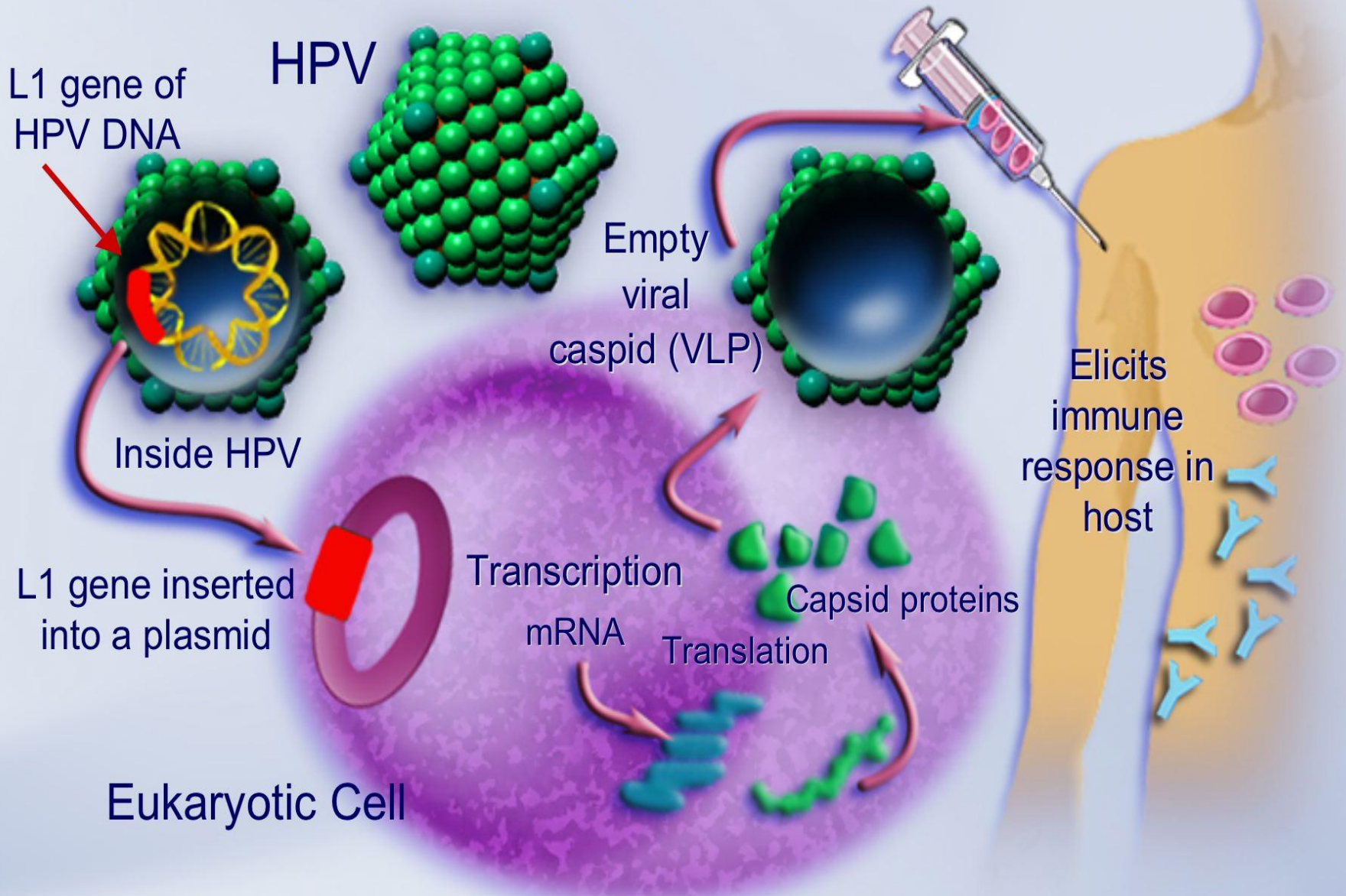
ACS Guidelines

- HPV & Cytology
 - After 30 yoa
 - Every 3 years
 - In combination with cytology
 - Repeat no more than q 3 yrs
 - Requires substantial counseling/education

How does the HPV vaccine work?

- Protects against 4 types of HPV
 - Types 16 & 18, responsible for 70% of cancers
 - Types 6 y 11, responsible for 95% of condyloma
- Stimulates “antibodies” that provide protection at the time of exposure to HPV
- Prevents HPV infection and subsequent development of pre cancer and cancer of the cervix

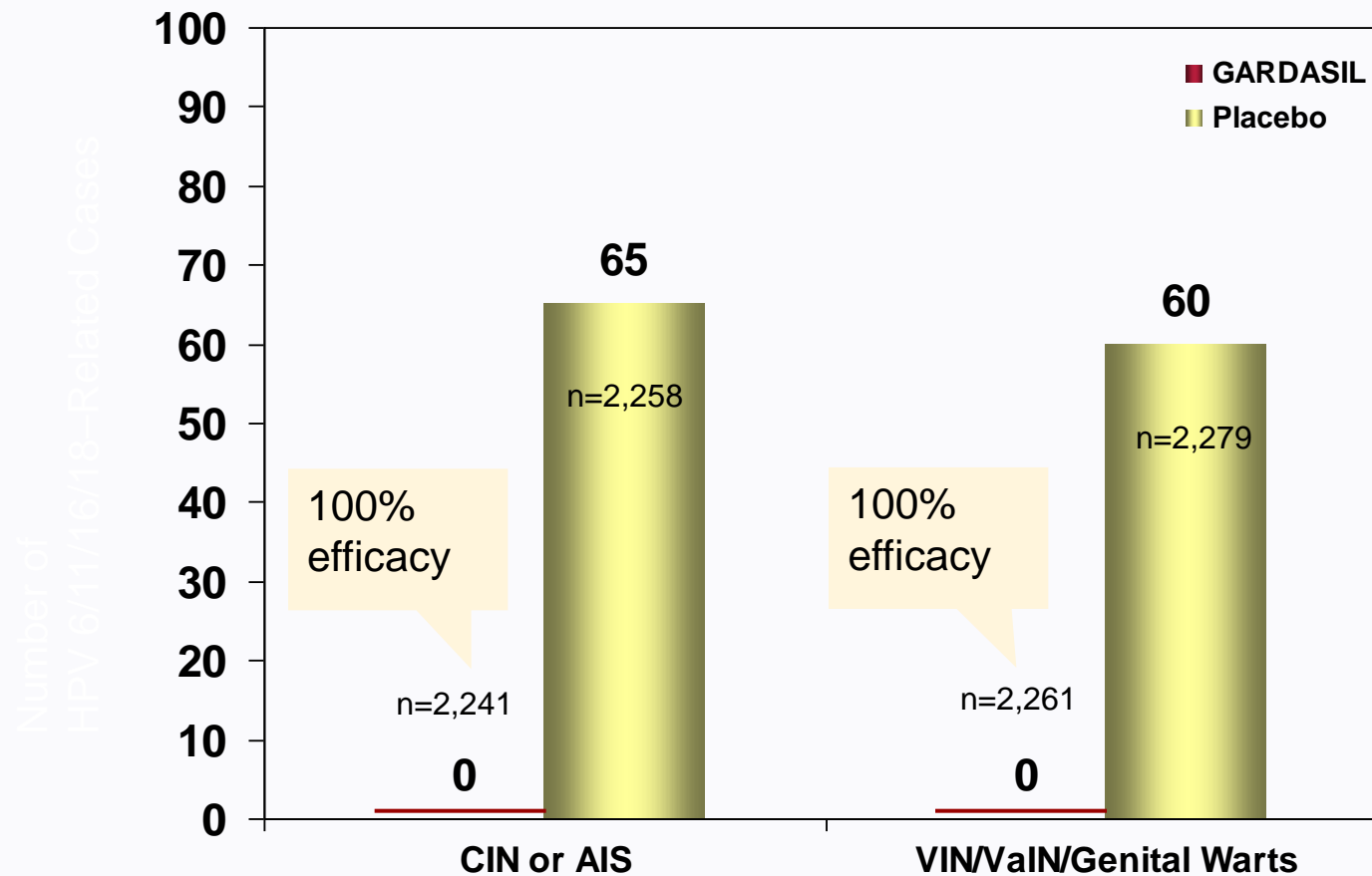
HPV L1 Virus-Like-Particle (VLP) Vaccine Synthesis



Vaccines: Summary

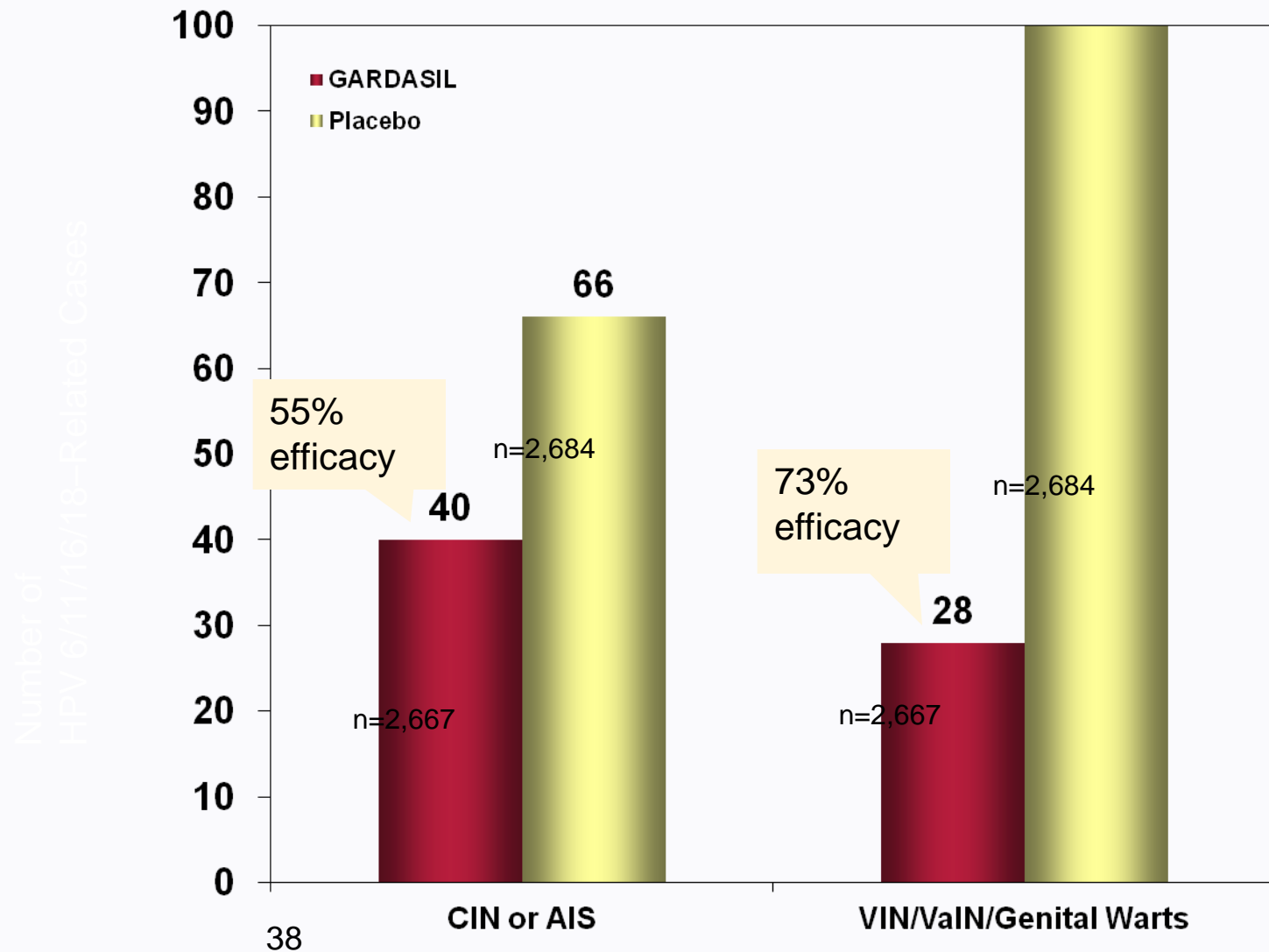
	Gardasil	Cervarix
	Merck	GSK
Expression	Yeast	Insect cells
Target HPV Genotypes	HPV6, 11, 16, 18	HPV16, 18
Vaccine Dose	0.5 mL: 20 µg HPV6, 40 µg HPV11, 40 µg HPV16, 20 µg HPV18	0.5 mL: 20 µg HPV16, 20 µg HPV18
Adjuvant	225 µg amorphous aluminum hydroxyphosphate sulfate	AS04: 50 µg 3-O-desacyl-4'-monophosphoryl lipid A and 0.5 mg aluminum hydroxide
Schedule	0, 2, 6 months	0, 1, 6 months
Efficacy (vs. HPV16/18)	>90%	>90%
Efficacy (vs. HPV31/45)	~40%	>90% (008 update at IPV meeting)

Efficacy of Vaccine for the Prevention of CIN & Condyloma in the per Protocol Population

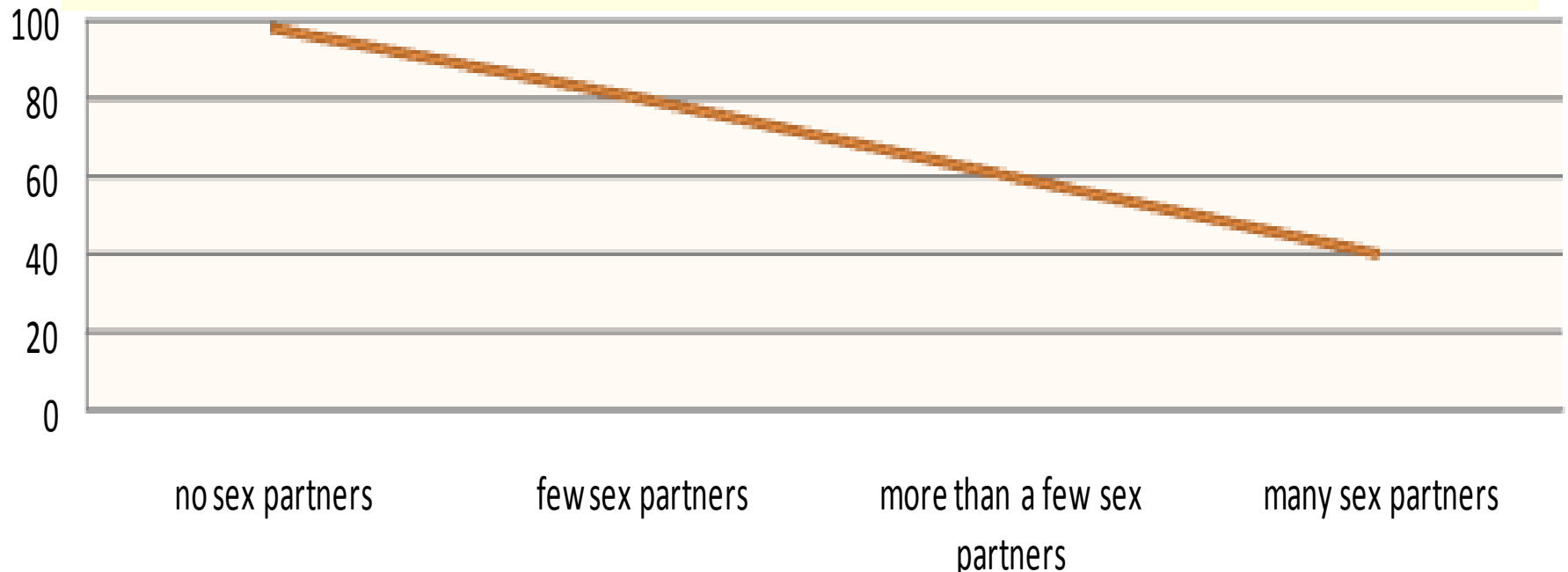


95% confidence interval: 94%–100%.

Efficacy of Vaccine for the Prevention of CIN & Condyloma in the Intent to Treat Population



Vaccine Efficacy Decreases with Number of Lifetime Partners



- HPV (type 16, 18, 6, and 11) infection risk decreases with vaccination prior to onset of sexual activity
- Infection with 4 vaccine types is rare, so there may be some benefit even with a history of sexual activity/HPV infection

American Cancer Society Recommendations for HPV Vaccination

- *Vaccinate girls/women up to the age of 18*
- *There are insufficient data to recommend universal vaccination of women 19 to 26*
- *In this group, the decision to vaccinate should be based on an informed discussion between the woman and her clinician.*

How do I decrease my risk of HPV infection and cervical cancer?

- ✓ Vaccinate prior to 19 years of age
- ✓ Delay onset of sexual activity
- ✓ Know your partner
- ✓ Use condoms
- ✓ Healthy lifestyle
 - avoid tobacco
 - healthy diet
- ✓ Screen regularly with Pap with/without HPV

Preventing Cervical Cancer

- Informed women
- Educated providers
- Access to screening and health care
- Cervical cancer should be entirely preventable
- One cervical cancer death is one too many

Francisco Garcia, MD, MPH

520 626 8539

fcisco@u.arizona.edu



Pima County Cervical Cancer Prevention Partnership

